Mallinckrodt to Present Data on TERLIVAZ® (terlipressin) for Injection in Adult Patients with Hepatorenal Syndrome (HRS) at the American Society of Nephrology (ASN) Kidney Week 2023 Scientific Meeting

November 1, 2023

–Three scientific abstracts via one oral and two poster presentations detail the Company's latest clinical research findings on the therapeutic effect of TERLIVAZ for adults with HRS involving rapid reduction in kidney function[1] –

DUBLIN, Nov. 1, 2023 /PRNewswire/ -- Mallinckrodt plc (OTCMKTS: MNKTQ), a global specialty pharmaceutical company, today announced that three scientific abstracts evaluating treatment with TERLIVAZ® (terlipressin) for injection for adults with hepatorenal syndrome (HRS) with rapid reduction in kidney function[1] – including its impact on patient care, key HRS endpoints and patient comorbidity – will be presented at the American Society of Nephrology (ASN) Kidney Week 2023 Scientific Meeting in Philadelphia, Pennsylvania, taking place November 2-5, 2023.

TERLIVAZ is the first and only FDA-approved product indicated to improve kidney function in adults with HRS with rapid reduction in kidney function,[1] an acute and life-threatening condition requiring hospitalization.[2]

Please see Limitation of Use and Important Safety Information, including Boxed Warning, below.

Mallinckrodt's three scientific abstracts at ASN's Kidney Week 2023 Scientific Meeting, two of which will take place on November 2 and one on November 4, will be presented by Juan Carlos Q. Velez, MD, and Hani M. Wadei, MD.

Juan Carlos Q. Velez, MD, will present findings from a post hoc analysis of the Phase III CONFIRM clinical trial exploring the incidence of HRS reversal in patients treated with TERLIVAZ plus albumin versus placebo plus albumin to determine if an improvement in serum creatinine of >30% was associated with improved clinical outcomes.[3] The study evaluated the magnitude of improvement in serum creatinine level from baseline to the end of treatment, and its potential relationship with patient's length of intensive care unit stay and the incidence of renal replacement therapy, among other clinical measures.[3]

A pooled analysis of the results from the three largest prospective, randomized, placebo-controlled clinical studies in patients with HRS (OT-0401, REVERSE, and CONFIRM) will be presented by Hani M. Wadei, MD.[4] The analysis assessed the role of TERLIVAZ plus albumin versus placebo plus albumin on HRS reversal in the subpopulation of patients with comorbidities of alcoholic hepatitis, mean arterial pressure of <70 mmHg and/or systemic inflammatory response syndrome.[4]

In an oral presentation, Hani M. Wadei, MD, will also present a post hoc analysis of the Phase III, randomized, placebo-controlled CONFIRM study evaluating the incidence, indications, and modes of renal replacement therapy used in the subgroup of patients with fluid overload, as determined by investigator assessment.[5] Patients with fluid overload included those who reported hemodynamic edema and effusions.[5]

Additional information on these studies can be found below.

"The CONFIRM clinical trial was the largest-ever prospective, randomized clinical trial of TERLIVAZ in patients with hepatorenal syndrome (HRS),[1] and continues to offer new learnings and insights as reflected in the upcoming presentations at the American Society of Nephrology's Annual Meeting," said **Khurram Jamil, Vice President, Hepatology, Clinical Development & Critical Care**. "We're hopeful these findings will continue to inform the medical community's approach to diagnosis and clinical management of this critical condition, leading to better outcomes for HRS patients with rapid reduction in kidney function."[1]

These studies are sponsored by Mallinckrodt Pharmaceuticals and include:

Abstract TH-PO052: Improvement in Serum Creatinine was Associated with Favorable Clinical Outcomes in Patients with Hepatorenal Syndrome: A Post Hoc Analysis of the CONFIRM Study[3]

- **Presenter:** Juan Carlos Q. Velez, MD, Ochsner Health, New Orleans, LA, USA
- **Session Type:** Poster Presentation
- **Presentation Location:** Exhibit Hall, Pennsylvania Convention Center
- **Session Date and Time:** Thursday, November 2, 2023; 10:00 a.m. – 12:00 p.m. EDT

Abstract TH-PO050: Terlipressin Therapy in Patients with HRS and Comorbidities: The North American Experience[4]

- **Presenter:** Hani M. Wadei, MD, Mayo Clinic, Jacksonville, FL, USA
- **Session Type:** Poster Presentation
- **Presentation Location:** Exhibit Hall, Pennsylvania Convention Center
- **Session Date and Time:** Thursday, November 2, 2023; 10:00 a.m. – 12:00 p.m. EDT

Abstract SA-OR03: Effect of Terlipressin Treatment on the Incidence of Renal Replacement Therapy in Patients with Hepatorenal Syndrome and Fluid Overload: A Post Hoc Analysis of the Phase 3 CONFIRM Study[5]

- **Presenter:** Hani M. Wadei, MD, Mayo Clinic, Jacksonville, FL, USA
- **Session Type:** Oral Presentation
- **Presentation Location:** Room 118, Pennsylvania Convention Center
- **Presentation Date and Time:** Saturday, November 4, 2023; 4:48 – 4:57 p.m. EDT

INDICATION AND LIMITATION OF USE

TERLIVAZ is indicated to improve kidney function in adults with hepatorenal syndrome with rapid reduction in kidney function.

- Patients with a serum creatinine >5 mg/dL are unlikely to experience benefit.

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS OR FATAL RESPIRATORY FAILURE

- **TERLIVAZ may cause serious or fatal respiratory failure. Patients with volume overload or with acute-on-chronic liver failure (ACLF) Grade 3 are at increased risk. Assess oxygenation saturation (e.g., SpO_2) before initiating TERLIVAZ.**
- **Do not initiate TERLIVAZ in patients experiencing hypoxia (e.g., SpO_2 <90%) until oxygenation levels improve. Monitor patients for hypoxia using continuous pulse oximetry during treatment and discontinue TERLIVAZ if SpO_2 decreases below 90%.**

Contraindications

TERLIVAZ is contraindicated:

- In patients experiencing hypoxia or worsening respiratory symptoms.
- In patients with ongoing coronary, peripheral, or mesenteric ischemia.

Warnings and Precautions

- **Serious or Fatal Respiratory Failure:** Obtain baseline oxygen saturation and do not initiate TERLIVAZ in hypoxic patients. Monitor patients for changes in respiratory status using continuous pulse oximetry and regular clinical assessments. Discontinue TERLIVAZ in patients experiencing hypoxia or increased respiratory symptoms.

  Manage intravascular volume overload by reducing or discontinuing the administration of albumin and/or other fluids and through judicious use of diuretics. Temporarily interrupt, reduce, or discontinue TERLIVAZ treatment until patient volume status improves. Avoid use in patients with ACLF Grade 3 because they are at significant risk for respiratory failure.

- **Ineligibility for Liver Transplant:** TERLIVAZ-related adverse reactions (respiratory failure, ischemia) may make a patient ineligible for liver transplantation, if listed. For patients with high prioritization for liver transplantation (e.g., MELD ≥35), the benefits of TERLIVAZ may not outweigh its risks.
- **Ischemic Events:** TERLIVAZ may cause cardiac, cerebrovascular, peripheral, or mesenteric ischemia. Avoid use of TERLIVAZ in patients with a history of severe cardiovascular conditions or cerebrovascular or ischemic disease. Discontinue TERLIVAZ in patients who experience signs or symptoms suggestive of ischemic adverse reactions.
- **Embryo-Fetal Toxicity:** TERLIVAZ may cause fetal harm when administered to a pregnant woman. If TERLIVAZ is used during pregnancy, the patient should be informed of the potential risk to the fetus.

Adverse Reactions

- The most common adverse reactions (≥10%) include abdominal pain, nausea, respiratory failure, diarrhea, and dyspnea.

Please click here to see full Prescribing Information, including Boxed Warning.

About Hepatorenal Syndrome (HRS)

Hepatorenal syndrome (HRS) involving rapid reduction in kidney function[1] is an acute and life-threatening condition that occurs in people with advanced liver disease.[2] HRS is classified into two distinct types – a rapidly progressive type that leads to acute renal failure where patients are typically hospitalized for their care and a more chronic type that progresses over weeks to months.[2] HRS involving rapid reduction in kidney function[1] is estimated to affect more than 35,000 Americans annually and rates of HRS hospitalizations are increasing.[6,7] If left untreated, HRS with rapid reduction in kidney function[1] has a median survival time of approximately two weeks and greater than 80 percent mortality within three months.[8]

ABOUT MALLINCKRODT

Mallinckrodt is a global business consisting of multiple wholly owned subsidiaries that develop, manufacture, market and distribute specialty pharmaceutical products and therapies. The company's Specialty Brands reportable segment's areas of focus include autoimmune and rare diseases in specialty areas like neurology, rheumatology, hepatology, nephrology, pulmonology, ophthalmology, and oncology; immunotherapy and neonatal respiratory critical care therapies; analgesics; cultured skin substitutes and gastrointestinal products. Its Specialty Generics reportable segment includes specialty generic drugs and active pharmaceutical ingredients. To learn more about Mallinckrodt, visit www.mallinckrodt.com.

Mallinckrodt uses its website as a channel of distribution of important company information, such as press releases, investor presentations and other financial information. It also uses its website to expedite public access to time-critical information regarding the company in advance of or in lieu of distributing a press release or a filing with the U.S. Securities and Exchange Commission (SEC) disclosing the same information. Therefore, investors should look to the Investor Relations page of the website for important and time-critical information. Visitors to the website can also register to receive automatic e-mail and other notifications alerting them when new information is made available on the Investor Relations page of the website.

CAUTIONARY STATEMENTS RELATED TO FORWARD-LOOKING STATEMENTS

This release contains forward-looking statements, including with regard to TERLIVAZ®, its potential to improve health and treatment outcomes, and its potential impact on patients. The statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those in the forward-looking statements: the impact of Mallinckrodt's pending Chapter 11 cases; satisfaction of, and compliance with, regulatory and other requirements; actions of regulatory bodies and other governmental authorities; changes in laws and regulations; issues with product quality, manufacturing or supply, or patient safety issues or adverse side effects or adverse reactions associated with TERLIVAZ; and other risks identified and described in more detail in the "Risk Factors" section of Mallinckrodt's most recent Annual Report on Form 10-K and other filings with the SEC, all of which are available on its website. The forward-looking statements made herein speak only as of the date hereof and Mallinckrodt does not assume any obligation to update or revise any forward-looking statement, whether as a result of new information, future events and developments or otherwise, except as required by law.

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References

[1] TERLIVAZ® (terlipressin) for injection. [Prescribing Information]. Mallinckrodt Hospital Products Inc. 2023.

[2] National Organization for Rare Disorders. Hepatorenal Syndrome. Available at: https://rarediseases.org/rare-diseases/hepatorenal-syndrome/. Accessed September 14, 2023.

[3] Velez JCQ, Mujtaba MA, Zhiwei Z, Elsiesy H, Jamil K. Improvement in Serum Creatinine was Associated with Favorable Clinical Outcomes in Patients with Hepatorenal Syndrome: A Post Hoc Analysis of the CONFIRM Study. *Abstract to be presented at the American Society of Nephrology (ASN) 2023 Annual meeting*. November 2023.

[4] Wadei HM, Zhang Z, Alzubaidl M, Jamil K. Terlipressin Therapy in Patients with HRS and Comorbidities: The North American Experience. *Abstract to be presented at the American Society of Nephrology (ASN) 2023 Annual meeting*. November 2023.

[5] Wadei HM, Mujtaba MA, Jamil K. Effect of Terlipressin Treatment on the Incidence of Renal Replacement Therapy in Patients with Hepatorenal Syndrome and Fluid Overload: A Post Hoc Analysis of the Phase 3 CONFIRM Study. *Abstract to be presented at the American Society of Nephrology (ASN) 2023 Annual meeting*. November 2023.

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[7] Singh J, Dahiya DS, Kichloo A, Singh G, Khoshbin K, Shaka H. Hepatorenal Syndrome: A Nationwide Trend Analysis from 2008 to 2018. *Annals of Med*. 2021; 53:1. doi.org/10/1080/07853890

[8] Flamm, S.L., Brown, K., Wadei, H.M., et al. The Current Management of Hepatorenal Syndrome–Acute Kidney Injury in the United States and the Potential of Terlipressin. *Liver Transpl*. 2021;27:1191-1202. https://doi.org/10.1002/lt.26072.

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